IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: BRENNAN et al. Group Art Unit: 1632

Serial No.: 09/892,206 Examiner: Bertoglio, Valerie E.

Filed: June 26, 2001 Attorney Docket No.: R-171

For: TRANSGENIC MICE CONTAINING ANAPHYLATOXIN C3A GENE DISRUPTIONS

RESPONSE TO RESTRICTION REQUIREMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Office Action mailed September 10, 2002, concerning the Examiner's restriction to the claims, Applicants hereby provisionally elect, with traverse, claims of Group III (claims 8, 17-25), drawn to a transgenic animal comprising a disruption in an anaphylatoxin C3a gene.

In the restriction, the Examiner asserts that claims 1-33 are drawn to seven distinct subjects, grouped as: Invention I (claims 1-4), drawn to a nucleic acid construct and methods of making the construct, classified in class 536, subclass 23.1; Invention II (claims 5-7, 9 and 27), drawn to cells with a disruption in an anaphylatoxin C3a receptor gene, classified in class 435, subclass 325; Invention III (claims 8, and 17-25) drawn to a transgenic animal comprising a disruption in an anaphylatoxin C3a gene, classified in class 800, subclass 13; Invention IV (claims 11, 12, and 28-30), drawn to methods of using a transgenic animal cell comprising a disruption in an anaphylatoxin C3a gene to test agents, classified in class 800, subclass 3; Invention V (claims 10 and 26) drawn to a method of making a transgenic animal, classified in class 800, subclass 21; Invention VI (claims 13-15, 31 and 32) drawn to methods of using cells with a disruption in an anaphylatoxin C3a gene to test agents wherein the cell is from a transgenic animal, classified in class 435, subclass 325; and Invention VII (claims 16 and 33) drawn to an agent, classified in class 530, subclass 350. Applicants respectfully request reconsideration and withdrawal of the requirement.

Specifically, the Examiner asserts that the claims of Groups I and II are patentably distinct because the nucleic acid construct can be used as a probe while the cells can be used in *in vitro* assays to determine agents that modulate anaphylatoxin C3a expression. The Applicants disagree with the Examiner's conclusion. Any search or examination of the prior art conducted on one of these aspects, *e.g.* production of anaphylatoxin C3a deficient transgenic animals, would produce results that would encompass the transgenic animals and the nucleic acid construct. Thus, the additional burden of a separate search or examination would not be required.

The Examiner further asserts that the claims of Groups I and III are patentably distinct because nucleic acid construct can be used as a probe while the transgenics can be used in *in vivo* assays to determine agents that modulate anaphylatoxin C3a expression. The Applicants believe that a reasonable search of the prior art would produce results related to anaphylatoxin C3a nucleic acid constructs and methods of identifying anaphylatoxin C3a modulators. A search and examination of the claims of each of these Groups, therefore, can be made without additional burden on the Examiner.

The Examiner also asserts that the claims of Groups I and IV are patentably distinct because nucleic acid construct can be used as a probe while the method can be used in *in vivo* assays to determine agents that modulate anaphylatoxin C3a expression. The Applicants disagree with the Examiner's assertion. A search or examination of the prior art conducted on the subject matter of Groups I and VI would produce results encompassing C3a nucleic acid constructs and methods of identifying anaphylatoxin C3a modulators. Thus, a search or examination of these claims would not seriously burden the Examiner.

According to the Examiner, claims of Group I and claims of Group V are related as product and process of use, respectively. The Examiner asserts that claims of Group I and Group V are patentably distinct because nucleic acid construct can be used in a materially different process, *e.g.* as a probe. The Applicants disagree with the Examiner's assertion. A search or examination of the prior art conducted on the subject matter of Groups I and V would produce results encompassing C3a nucleic acid constructs and methods making a anaphylatoxin C3a-disrupted transgenic animal. Thus, a search or examination of these claims would not seriously burden the Examiner.

It is also asserted by the Examiner that the claims of Group I and Group IV are patentably distinct in that the construct of Group I can be used as a probe while the methods of Group ~~IV~~ VI?

can be used to determine agents that modulate anaphylatoxin C3a expression. The Applicants disagree with the Examiner's conclusion. The Applicants believe that a reasonable search of the prior art would produce results related to anaphylatoxin C3a nucleic acid constructs and methods of identifying anaphylatoxin C3a modulators. A search and examination of the claims of each of these Groups, therefore, can be made without additional burden on the Examiner.

The Examiner further asserts that the claims of Group I and Group VII are patentably distinct because the nucleic acid construct can be used as a probe while the agent can be used to modulate anaphylatoxin C3a expression. The Applicants disagree with the Examiner's conclusion. The Applicants believe that a reasonable search of the prior art would produce results related to anaphylatoxin C3a nucleic acid constructs and agents that modulate C3a expression. A search and examination of the claims of each of these Groups, therefore, can be made without additional burden on the Examiner.

The Examiner further asserts that the claims of Groups II and either of Groups III or IV are patentably distinct because the cells of Group II can be used to determine differential gene expression while the transgenics or methods, respectively, can be used for different purposes with protocols and reagents that are materially distinct. The Applicants disagree with the restriction of the cells of Group II from the transgenics or methods because these two groups are related and would therefore product related search results. Thus, the Applicants respectfully assert that the claims of Group II should be examined together with the claims of Groups III and IV.

According to the Examiner, the claims of Group II and Group V are related as product and process of use, respectively. The Examiner asserts that Group II and Group V are patentably distinct because cells can be used in a materially different process, *e.g.* in *in vitro* assays to determine agents that modulate anaphylatoxin C3a expression. The Applicants disagree with the Examiner's conclusion. A search or examination of the prior art conducted on the subject matter of Groups II and V would produce results encompassing the cells comprising a disruption in a anaphylatoxin C3a gene and methods making a anaphylatoxin C3a-disrupted transgenic animal using such cells. Thus, a search or examination of these claims would not seriously burden the Examiner.

Similarly, Group II and Group VI are asserted by the Examiner to be related as product and process of use, respectively. Specifically, the Examiner asserts that the methods of testing

agents of Group VI can be done *in vivo* while the cells of Group II can be used in *in vitro* assays. The Applicants disagree with the Examiner's assertion. In particular, the Applicants respectfully point out that the Examiner has classified the claims of Group II and Group VI in the same class and subclass (class 435, subclass 325). A search or examination of the prior art conducted on the subject matter of Groups II and VI would produce results encompassing the cells comprising a disruption in a anaphylatoxin C3a gene and methods of testing agents using such cells. Thus, a search or examination of these claims would not seriously burden the Examiner.

The Examiner further asserts that Group II and Group VII are patentably distinct because cells of Group II can be used in *in vitro* assays to determine differential gene expression while the agent can be used to modulate anaphylatoxin C3a. The Applicants disagree with the Examiner's assertion. A search or examination of the prior art conducted on the subject matter of Groups II and VII would produce results encompassing the cells and the agents. Therefore, undue burden on the Examiner would not result from a search and examination of the claims of Groups II and VII.

According to the Examiner, the claims of Group III and Group IV are related as product and process of use, respectively. Specifically, the Examiner asserts that the methods of testing agents of Group VI can be done *in vitro* while the transgenic of Group III can be used to determine the role of anaphylatoxin C3a *in vivo*. The Applicants disagree with the Examiner's conclusion. Any search of the prior art related to, *e.g.* methods of using cells with a disruption in an anaphylatoxin C3a gene would include results that include transgenic animals comprising such a disruption.. A search and examination of the claims of Group III and Groups IV can be made without serious burden on the Examiner.

According to the Examiner, Group III and Group V are related as product and process of use, respectively. The Examiner asserts that the Groups are distinct because transgenic mouse of claim III can be made by a materially different process, *i.e.*, by injecting the blastocyst with DNA. Applicants respectfully disagree with this conclusion. As is well known in the art, the rate of homologous recombination does not permit injection into a blastocyst when making a transgenic comprising a disruption in a gene. In contrast to transgenic mice wherein the DNA is simply taken up by a blastocyst and may be expressed, the disruption of a gene must be accomplished by introducing a construct into a cell in tissue culture, whereupon the process of detecting the extremely rare event of a disrupted gene can be accomplished under selective

pressure. Furthermore, Applicants assert that any search of the prior art related to, *e.g.* methods of using cells with a disruption in an anaphylatoxin C3a gene would include results that encompass transgenic animals comprising such a disruption. A search and examination of the claims of Group III and Groups V can be made without serious burden on the Examiner.

It also asserted by the Examiner that the claims of Groups III and those of either of Groups VI or VII are patentably distinct because the transgenics of Group III can be used to determine the role of anaphylatoxin C3a *in vivo* while methods of using the cells of Groups VI are process steps with the purpose of identifying agents, and the agent of Group VII is used to modulate anaphylatoxin C3a. According to the Examiner, the burden to search the transgenics along with either the methods of using cells and or agents would be undue. The Applicants disagree with the Examiner's conclusion. The Applicants do not believe that an undue burden would be placed on the Examiner in order to search the prior art regarding the transgenics comprising a disruption in an anaphylatoxin C3a gene and either methods of using cells comprising the same disruption or agents identified by using the cells.

The Examiner also asserts that the methods of each of Groups IV-VI are materially different and plurally independent from each other because each is practiced with materially different process steps and for different purposes. The Applicants respectfully submit that methods of using a transgenics comprising a disruption in an anaphylatoxin C3a, methods of making said transgenic, and methods of using a cell from said transgenic are sufficiently related as to be encompassed by a search that would not place an undue burden on the Examiner.

The Examiner also asserts that the claims of Group IV and those of Group VII are patentably distinct because the agent can be identified from *in vitro* assays using cells harboring a disruption in anaphylatoxin C3a without using the transgenic. Applicants respectfully argue that an *in vitro* assay using cells harboring a disruption in anaphylatoxin C3a is sufficiently related to a transgenic comprising a disruption in anaphylatoxin C3a as to impose a burden upon the Examiner that would not be undue despite the differences in structure between the transgenic and the agent.

The Examiner also asserts that the claims of Group V and those of Group VII are patentably distinct because the methods used to generate the transgenic differ from those associated with the agent are distinct and separate, each not requiring the other and each having materially different structures. Applicants respectfully argue that agents identified using

transgenic animals comprising a disruption in anaphylatoxin C3a gene or cells comprising a disruption in an anaphylatoxin C3a gene are related to methods of making the transgenic *visa vis* the disruption in an anaphylatoxin C3a gene. Thus, it would not be unreasonably burdensome to search both the agent and the methods.

Finally, with respect to the claims of Group VI and Group VII, the Examiner concludes that the Groups are patentably distinct because the agent does not require the methods of using cells and the methods do not require the agent. The Applicants disagree with the Examiner's conclusion. Any search or examination of the prior art related to the subject matter of Group VI and Group VII can be made without serious or undue burden on the Examiner.

Although Applicants have provisionally elected Group III for purposes of advancing prosecution of the present application, Applicants contend, for the foregoing reasons, that the restriction requirement is improper. Accordingly, Applicants respectfully request reconsideration and withdrawal of the requirement.

Respectfully submitted,

Date: 16 Dec. 2002

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Enclosures

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ENCLOSURES *(check all that apply)*

- [ ] Fee Transmittal Form
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- [XX] Amendment / Reply /Restriction
- [ ] After Final
- [ ] Affidavits/declaration(s)
- [XX] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
- [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Assignment Papers *(for an Application)*
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] After Allowance Communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
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Remarks

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